

Identifying Gaps in Knowledge and Next Directions for MATE Transporters

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Multidrug and Toxin Extrusion proteins (MATE, SLC47A) are efflux transporters that excrete drugs and xenobiotics, contributing to renal and hepatic elimination. In the kidneys and liver, MATEs regulate the apical secretion of compounds into urine and bile. Since their discovery in 2005, there has been emerging interest in the role of MATEs on mediating drug-drug interactions and influencing therapeutic outcomes. The purpose of this study was to analyze primary literature regarding MATE transporters to 1) identify gaps in knowledge and 2) assemble comprehensive lists of substrates and inhibitors. The search terms “MATE1 or MATE2K or SLC47A1 or SLC47A2” on PubMed identified 397 published manuscripts, which were filtered to 239 English original research studies on mammalian isoforms by reviewing titles and abstracts. The 239 publications were categorized by study type (i.e., in vitro/ in silico, in vivo animal, and clinical/ specimens) and topic (e.g., Drug-Drug Interactions, Pharmacogenetics, Identifying Substrates, Identifying Inhibitors, Expression and Regulation, Toxicity, and Structure-Function). Studies were also used to construct comprehensive tables of MATE substrates and inhibitors. Regarding study type, 40% were in vitro/ in silico studies, 16% were in vivo animal studies, 23% were clinical/ specimen studies, and 21% used a combination of in vitro, in vivo, and/or clinical studies. Assessment of study topics revealed the following breakdown: 17% Drug-Drug Interaction, 14% Pharmacogenetics, 16% Substrates, 17% Inhibition, 27% Expression and Regulation, 6% Toxicity, and 3% Structure-Function. Notably, some publications covered multiple topics. Results identified that most studies have focused on expression and regulation of MATE transporters, with little exploration on the structure and toxicology. These data suggest that future studies in this area should aim to elucidate the structure of MATE transporters and determine how MATE-mediated interactions can cause poor therapeutic outcomes, including risk of adverse effects. Funded by NIH GM123330, ES005022, CA072720, CA046934, ES020721, and ASPET Fellow Program.

